Conseil *d'*Évaluation *des* Technologies *de la* Santé *du* Québec

Report – June 2000
(CETS 2000-1 RE)

IMPLANTABLE VENTRICULAR ASSIST DEVICES: SHOULD THEY BE USED IN QUÉBEC?

Report submitted to the Minister of Research, Science and Technology of Québec

Conseil d'évaluation des technologies de la santé du Québec

Information concerning this report or any other report by the *Conseil d'évaluation des technologies de la santé* can be obtained by contacting the *Conseil* 's office:

Conseil d'évaluation des technologies de la santé
2021, avenue Union, bureau 1040
Montréal (Quebec) H3A 2S9

Telephone: (514) 873-2563
Fax: (514) 873-1369
E-mail: cets@mrst.gouv.qc.ca
Web site address: http://www.cets.gouv.qc.ca

Legal deposit	-	*Bibliothèque nationale du Québec*, 2000
	-	National Library of Canada
ISBN		2-550-36174-1

How to cite this document:

Conseil d'évaluation des technologies de la santé du Québec. Implantable Ventricular Assist Devices: Should They Be Used in Quebec? (CETS 2000-1 RE). Montreal: CETS, 2000, viii-36 p. (Original French version published in March 2000).

SUMMARY

INTRODUCTION

Heart failure is common. Until recently, when medication was no longer able to maintain function, life could only be prolonged by cardiac transplantation. However, very few donor hearts are available each year.

Mechanical pumps have now been developed which can be implanted in the body of the recipient and take over the heart's function, thus prolonging life for months or years. These devices are being used in Europe and the USA but have only had very limited application in Canada and Quebec.

The present document reviews the available data pertaining to the decision whether they should now be used in Québec. It originally arose from a request by the *Régie régionale de la santé et des services sociaux de Montréal-Centre*; however, as the issue concerns the entire province, the *Ministère de la Santé et des Services sociaux du Québec* is very interested in the results of this evaluation.

Status of Technology

This is a new and rapidly developing technology but is no longer experimental. It is appropriate to consider it an "innovative" technology and as such, consider its application within the strict framework of data collection for research purposes.

Applications

Left ventricular assist devices (LVADs) are used in emergency situations where, in their absence, the outcome would be imminent death. They are also used electively in the context of progressive heart failure. LVADs may be used with three objectives: as a bridge to transplantation, as a bridge to recovery, or as a permanent alternative to transplantation.

Efficacy

The following estimates of outcome are no more than approximations, based on the results of the more recent reports:

Survival to transplantation or explantation can be expected for approximately 70% of implanted patients. In elective cases, prior LVAD use may improve *transplant* survival rates at 5 years from approximately 70% to possibly as high as 90%.

Hemorrhage requiring re-operation may occur in 20-44% of patients in the first few post-operative days, but is rare thereafter.

Thromboembolism rates have varied from 5-15% (HeartMate®) to 12-37% (Novacor®). The lower rates, 5% and 12%, are probably more pertinent to the present decision.

Infections, either systemic or local, are experienced by approximately 50% of patients. Both thromboembolism and infection are encountered throughout the duration of the implant but their frequency diminishes with time.

Quality of Life. Many patients on long-term LVAD support can return home and resume a near normal life, taking part in work and recreational activities. Overall, quality of life is superior to that of a patient in advanced heart failure but inferior to that of a transplant survivor.

Costs of implantation

The direct cost to the Canadian health care system of installing a Novacor® LVAD is approximately $138,000. Assuming 70% survival to transplant with an average 100 days support, this

technology would increase the cost of each cardiac transplantation by approximately $200,000.

Cost-effectiveness

It is premature to attempt precise estimates of cost-effectiveness. First approximations based on hypothetical scenarios, considering only direct costs to the health care system, provide the following estimates:

- Bridge to transplant, *emergency interventions* for cardiogenic shock: No estimate possible. No additional lives saved.

- Bridge to transplant, *elective interventions* for patients awaiting transplantation: Estimates range from $91,000 to $126,000 ($117,000 to $186,000 discounted at 5%) per life year.

- Permanent alternative to transplantation. *Emergency use*: $52,000 (discounted: $50,000) to $60,000 (discounted: $58,000) per life year. *Elective use*: $71,000 (discounted: $68,000) per life year.

Economic Impact

If employed *strictly* as a bridge to transplant and so used before 10 transplant procedures per year, the total annual cost, exclusive of transplantation related costs, would be of the order of $1.4 million. Some implants will, however, become permanent, causing an increasing cost. If 4 of the 10 patients receiving LVADs remain on permanent LVAD support, the total cost, exclusive of transplantation costs, by the end of 12 years might be approximately $3.8 million per year. If used as a permanent substitute for transplantation for 1,500 patients each year, the annual expenditure after 12 years might be of the order of $570 million (while sustaining the lives of perhaps 9,500 patients).

Ethical and Social Considerations

Consideration of the ethical and social issues leads to the following tentative conclusions:

- It is no longer ethically acceptable to refuse all access to this demonstratedly effective technology on grounds of cost alone.

- On the other hand, it would not be ethical to approve its extensive use until the economic demands of substantially more cost-effective technologies have been addressed.

- If used only as a bridge to transplantation, to rescue cases in cardiogenic shock who would otherwise have a rapidly fatal outcome, 10 LVADs might be required in the first year. It would be reasonable to initially limit LVAD use to this number.

- Until there is a substantial increase in the effectiveness of this procedure and a reduction in its cost, its application with the intent of providing a permanent substitute for transplantation would lead to inappropriate use of resources.

- It will be difficult to limit the use of this technology. There will be social, political and medical pressures to expand its use to all individuals whom it might benefit. It is essential that the number of implants authorized be clearly defined in advance.

Significant Practical Issues

Initiation of this technology should not be undertaken without prior decisions being taken on the following issues:

Research. A major reason for proceeding to use LVAD technology would be to contribute to knowledge. The first objective should be a comparison of the outcomes and costs of the technol-

ogy with conservative management. The relevant clinical and cost data of every case implanted in Quebec should therefore be recorded in a registry with all the rigor of a research study, and a matching control series should be established. Delivery of such research data should be a condition of approval.

Centralization. To maximize the acquisition of skills, LVAD technology should initially be concentrated in a single centre which already carries out heart transplantation and which offers access to all medical specialty services.

Access. To facilitate access, the centre undertaking LVAD technology should establish a functional communications network with other cardiac surgical centres. Some of these should be equipped with devices such as Abiomed® or Thoratec® to facilitate rescue and transport of cases. To receive transfers the implant centre would need to maintain a heart failure unit with appropriate beds and support staff.

Budget. Existing budgets will not be able to absorb the cost of this new technology. If it is to be undertaken, appropriate funding must be provided outside existing hospital budgets.

Evaluation. The program should undergo thorough evaluation at regular intervals (initially at least every 3 years). At this time, possible extension of the program, or other modifications, must be decided upon. Poor clinical results or failure to produce the research data should be considered cause for transfer of the program elsewhere.

Importance of a Public Debate

Access to an effective technology has not, until at least recently, previously been limited on grounds of its cost. Until the opportunity costs of such decisions (i.e. what we must do without in order to pay for a technology like LVADs) are understood and widely accepted, wise decisions will be difficult to make and apply. In order for the public to comprehend and accept these decisions, there must be widespread and open debate of the fundamental issues raised by allocation of collective resources.

ACKNOWLEDGEMENTS

This report was prepared at the request of the *Conseil d'évaluation des technologies de la santé du Québec* by **Maurice McGregor**, MD, cardiologist and researcher-consultatn for the *Conseil*. We wish to express our gratitude to him for the work done.

The *Conseil* also cordially thanks the external reviewers for their many comments, which helped improve the quality and contents of this report:

James Brophy	Cardiologist, Department of Cardiology, Centre hospitalier universitaire de Montréal – Hôpital Notre-Dame, Montréal (Québec)
Daniel Doyle	Heart surgeon, Head, Surgery, Heart Transplantation Program, Hôpital Laval, Québec (Qc)
Anne Lemay	Economist, Association des hôpitaux du Québec, Montréal (Québec)
Jocelyne Saint-Arnaud	Associate Professor, Faculté des sciences infirmières, Université de Montréal, Montréal (Québec)
Michel White	Cardiologist, Research Centre, Montreal Heart Institute, Montréal (Québec)

We also wish to call attention to the invaluable contribution of Fatiha Rachet, cardiologist and research-consultant for the *Conseil*, who reviewed this report.

Lastly, the *Conseil* expresses its gratitude to Marc-André Thibodeau, library technician, and Pierre Vincent, librarian, for their bibliographic support, and Maria-Edith Jacques, for the final layout of this report.

TABLE OF CONTENTS

1. INTRODUCTION

Heart failure is a common cause of invalidism and death with a reported prevalence in the USA of between 1.1% and 2.0% of the noninstitutionalized population between 25 and 75 years of age [53]. Much effort has been spent on developing mechanical devices designed to replace the heart or to support the function of one or both of its ventricles. Earlier devices such as the cardiopulmonary bypass apparatus, the balloon counterpulsation device, or externally placed centrifugal pumps, were developed to sustain the circulation for a few hours or days. Subsequently, increasingly practical pumps were developed, which were capable of sustaining the circulation for months or years.

Some of these devices, such as the CardioWest TAH® are mechanical hearts which completely replace the native heart and are placed in the cardiac space in the thorax. Others called ventricular assist devices (VADs) are pumps which accept blood from either or both ventricles, returning it under pressure to the aorta or pulmonary artery. Some of these, such as the Abiomed BVS 5000® or the Thoratec® VAD, are placed outside the body, the most recent version of the latter being portable and allowing considerable mobility. In two, the Novacor® (Baxter HealthCare) and the HeartMate® (Thermo Cardiosystems Inc.), the pumps are implanted in the body, in the anterior abdominal wall or upper abdomen respectively, with only a power line penetrating the body's surface. Though usable for right or left ventricular support, the greatest experience has been accumulated in the use of these two implantable devices to support left ventricular function (implantable LVADs). Because of this, and because of their portability and potential to permanently substitute for the failed ventricle, they will be the devices principally considered in this assessment report.

These devices have been the subjects of excellent recent reviews [17, 22] and three previous technology assessments [25, 41, 61]. The object of the present study is not to repeat these reviews or to compare the presently available makes of implantable VAD with each other. It is rather to consider the overall efficacy, the costs, and some of the ethical and social issues associated with use of this technology for long-term cardiac support, focussing in particular on those data which are relevant to the decision whether or not implantable LVADs should be used in adults in Quebec at this time.

2. METHODS

There is as yet no relevant evidence concerning the use of VADs which is based on randomized clinical trials. Some data derive from the developers of the devices. A little evidence is based on poorly controlled comparative case series, and most is derived from case series of variable quality.

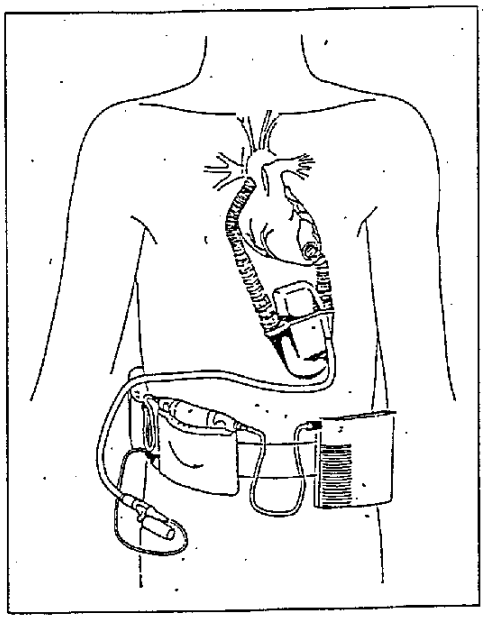
The present review borrows from recent technology assessments carried out in France by the *Comité d'Évaluation et de Diffusion des Innovations Technologiques* (CEDIT) for the *Direction de la Politique Médicale* de l'*Assistance Publique des Hôpitaux de Paris* [25], in the USA by the Oregon Health Resources Commission [41], and in the United Kingdom by the Wessex Institute [61] as well as the reviews of Hunt et al [22], and Goldstein et al [17]. It also uses information obtained through use of the MEDLINE data base (January 1, 1993 to December 1, 1999) using key words "VAD" and "mechanical circulatory support", references cited in all of the above sources, papers presented at the Meeting on Mechanical Cardiac Support and Replacement of the International Society for Heart and Lung Transplantation (ISHLT), Atlanta, November 5-6, 1999, and information supplied by the Novacor Division of Baxter HealthCare Corporation, Thermo Cardiosystems Inc., Abiomed Inc., and Thoratec Laboratories. Since the technology is evolving rapidly, evaluation of clinical efficacy is based principally on reports appearing since 1994.

3. THE IMPLANTABLE LVAD

3.1 DESCRIPTION

The LVADs under consideration are implanted surgically using cardiopulmonary bypass. The Novacor®, which is illustrated in Figure 1, is implanted in the abdominal wall behind the rectus abdominis muscle with only a power line penetrating the skin, while the externally similar HeartMate® devices are positioned in the abdomen behind the rectus muscle. Conduits drain blood from the left ventricle to the pump and return it to the ascending aorta. In this way, the function of the left ventricle can be partially or completely taken over by the device.

Figure 1: Simplified representation of the Novacor® LVAD



Following surgical implantation, the pumps are controlled by bedside consoles, which have both programming and monitoring capacity, and provide power to the units. When patients are mobilized, the Novacor® and HeartMate® electric pumps are connected to portable systems consisting of a small portable controller and rechargeable power packs, all worn on the patient's belt or suspended in a shoulder bag. At night or when patients are immobile, the pump units are connected to a small "personal" power source.

3.2 MECHANICAL RELIABILITY

Mechanically these devices are reasonably reliable. Twelve Novacor® units which underwent *in vitro* testing to failure between April 1994 and December 1998, averaged 4.2 (max 5.6) years of operation per unit. All functioned for over 3 years without developing any problems[1].

By February 1999, 635 current Novacor® units had been successfully implanted, with a cumulative 226 years of experience (information provided by Dr. Portner: see note 1). In 25 patients with a median duration of support of 1.6 years, connector wearing out occurred in 4 cases and recipient induced guideline damage in 3. All were successfully managed [24]. The manufacturer believes the Novacor® units will have a trouble-free functioning life of approximately 4 years though this estimate is not yet based on clinical experience (according to Dr. Portner).

By October 1999, 1,157 patients had received the HeartMate® pneumatic powered device (IP), and 777 the electrically powered device (VE). Of these 1,934 patients, 301 were supported for over 180 days and 65 for more than one year. Though device failures were reported with the earlier pneumatic device [34] none have been reported

[1] Information provided by P.M. Portner, MD, Stanford University School of Medicine, Stanford, CA, USA, 1999.

from use of the electric device since its approval in October 1998[2].

[2] Personal communication with N. Mastrangelo of Thermo Cardiosystems Inc., Woburn, MA, USA, 1999.

4. APPLICATIONS OF LVADS

Implantable LVADs are used under conditions of *varying urgency* ranging from emergency to elective, and with *three different objectives.*

4.1 URGENCY

Emergency Implantation

Sudden loss of ventricular function, so severe that blood pressure cannot be maintained, occurs in the context of massive myocardial infarction or following cardiac surgery. In either situation, in addition to maximal medication, the circulation is usually supported as necessary by balloon counterpulsation or by a centrifugal VAD. When a patient cannot be weaned from these devices after a few days, recovery becomes increasingly unlikely unless a donor heart becomes available. Life can then be maintained by use of a long-term LVAD [10]. We will refer to this situation as *emergency implantation.*

Elective Implantation

LVADs are more frequently used in the context of slow deterioration of cardiac function in a patient awaiting cardiac transplantation. An implantable LVAD may then be used to sustain life until a donor heart becomes available, or in the case of very advanced failure, to improve the chance of survival when a donor organ does become available. This situation arises when severe long-standing cardiac failure has depressed the function of the liver or kidneys, or caused drug resistant pulmonary hypertension, or resulted in body wasting and general depression of function so as to make successful cardiac transplantation unlikely. LVAD-assisted circulation with restoration of cardiac output can then greatly improve clinical status and survival [3, 13, 15]. Although there may be considerable urgency in some of these cases, the timing of implantation can usually be chosen and they will be referred to as *elective implantation.*

4.2 APPLICATIONS

LVADs can be used with three very different objectives in mind:

- As a bridge to transplant, to sustain life until a donor heart becomes available.
- As a bridge to recovery, with the objective of resting the failed ventricle in the hope that it will recover sufficiently to allow eventual explantation of the device.
- As an alternative to transplantation, remaining implanted “permanently”, to be replaced only when necessary by a new unit.

4.2.1 Bridge to Transplant

There is now wide agreement on the clinical efficacy of this technology when used for the first objective [10, 15, 17, 18, 25]. In the emergency situation there is seldom a suitable donor heart immediately available. In the elective situation also, because the need for donor hearts greatly exceeds supply, it frequently occurs that clinical deterioration makes transplantation urgent in the absence of a donor heart.

It must be noted that when LVADs are restricted to the bridge to transplantation application, few, if any, additional lives will be saved through their use, since the limiting factor is the number of donor hearts available. While the life of a patient who would have died may be saved by use of the device, due to the shortage of donors, when these patients progress to transplantation, some other individual on the transplant waiting list is deprived of their chance of survival. Thus this use of the technology does not, except as

discussed below, save new lives but only different lives.

4.2.2 Bridge to Recovery

The most desirable outcome is when the circulatory assistance results in reversal of medically-resistant pulmonary hypertension [1] or recovery of the failed ventricle [31, 38] to the extent that the native heart functions satisfactorily after device explantation.

Unfortunately this is not a frequent event. For example, it has been reported in 3.5% of 85 patients supported by LVAD (HeartMate®) [9], and in 2% of 1,387 patients implanted with the same device [14]. In a retrospective review of 111 LVAD implants, explantation without transplantation was possible in 4.5% of patients [32]. However, it is possible that with the acquisition of greater skill in weaning, more patients may be successfully explanted in the future. Using frequent measurements of cardiac function and careful timing, Mueller has recently reported on a cohort of 107 patients with dilated cardiomyopathy treated with LVAD since 1966, of whom 24 (22%) were successfully weaned, and 14 (13%) showed lasting recovery [37].

4.2.3 Alternative to Transplant

By contrast with the bridge to transplant application, the use of LVADs as a permanent alternative to transplantation is more contentious. The CEDIT evaluation explicitly recommends that "the extension of their use to other indications (than bridging to transplant) cannot yet be evaluated" [25].

The Oregon Health Resources Commission is even more restrictive in its approval, limiting LVAD application to "bridge-to-transplant support for properly selected transplant patients who are already on a transplant waiting list at a certified transplant centre". LVADs should not, they conclude, be used "for patients who are not already on such a waiting list" even if they subsequently become "transplant eligible" [41].

The Oregon report further stipulates that "The panel believes at this time that VADs should not be used with patients for whom there is no reasonable expectation of either being able to successfully transplant (after bridging to transplant) or to successfully wean and explant (after sufficiently bridging to recovery over not too long a period until recovery). In other words, at this point, if there is no reasonable expectation of being able to remove the device following transplantation or a not too long-term recovery period, it should ordinarily not be implanted". In summary, they conclude that "VADs cannot be recommended for longer-term bridge to recovery for chronic heart failure patients, nor as destination therapy in place of transplantation" [41].

The reasons for both the French and Oregon evaluators limiting their approval of VADs to application 1, bridge to transplant, are important. The reason for the Oregon group to further exclude their long-term use even for this function is possibly because their decisions may have been influenced by reports of use of an early version of the HeartMate®. There was clearly concern for the lack of evidence of long-term use at this time, with uncertainty as to the quality of life to be expected by long-term users. The Oregon group also had major concerns as to the potential economic impact of approval of this technology.

By contrast with these evaluations, several authors have expressed the opinion that this technology is now sufficiently advanced to allow consideration of its application with the objective of permanent support [6, 19, 42, 44].

CLINICAL RESULTS OF LVAD APPLICATION

5.1 GENERAL DATA

Fairly extensive experience of implantable LVAD use has now been accumulated. By April 1999, Novacor® units had been implanted in 1,074 patients for an average duration of 103 days. Of these patients, 54% had proceeded to transplantation, 2% had been successfully explanted, 7% were still implanted at the time of reporting and 37% had not survived. The median duration of support was 153 days, with 38 supported for over 6 months and 17 over 1 year[3]. By September 1999, 1,934 patients had been implanted with one or other of the HeartMate® devices. Of 777 patients supported by the electrically powered device (HeartMate® VE) for an average 114 days, 131 were still ongoing. Of the remaining 646, 266 (41%) had expired prior to transplantation, 358 (55%) had been successfully transplanted, and 22 (3.4%) had been explanted [58].

We will attempt below to arrive at estimates of the health and economic consequences which can be expected from use of implantable LVADs at this time. These consequences can only be meaningfully considered in comparison to the consequences of *not* using these devices. However, apart from the situation of emergency implantation when the alternative is rapid demise, the outcomes of comparable cases treated medically, let alone randomized studies, are not available. Thus, the following estimates are of necessity based on descriptive case series carried out in different centres, using different techniques with differing case selection, and all estimates must be considered first approximations and treated with great caution. Nevertheless, to arrive at policy decisions, even if they be short-term and subject to revision in the near future, some estimates of the outcomes which may be expected are essential.

[3] Information provided by P.M. Portner, MD, Stanford University School of Medicine, Stanford, CA, USA, 1999.

5.2 SURVIVAL RATE

There is reportedly great variation in outcome from centre to centre after LVAD implantation both in US (according to Dr. Portner: see note 3) and European [12] centres. In addition to between centre differences, the survival rate is heavily influenced by the severity of the cases selected. Appropriate use of this technology in the setting of otherwise irreversible cardiogenic shock is clearly capable of saving lives. For example, De Rose and colleagues reported on 12 postoperative patients selected because of failure to wean from bypass, or unresponsiveness to inotropic support, or balloon counterpulsation. Of these patients who normally would have died, 9 survived and were discharged from hospital [10]. Lives can also clearly be saved when LVADs are used more electively to sustain the life of a rapidly deteriorating patient who urgently requires a transplant, but no donor organ is available. It is reasonable to assume near 100% mortality for such cases in the absence of LVAD use. Their value when used to improve the health of the recipient, and thus the probability of successful transplant, can be accepted but is harder to quantitate.

Overall survival

To derive an overall value for survival is not easy. Of the first 993 patients treated worldwide with one of the HeartMate® devices, 59% survived to transplant or recovery [45]. In a US series of 100 patients in which HeartMate® devices were implanted, 76 survived to transplantation [34]. In another series of 85 patients receiving the same device, 73% survived to transplant

or explant [19], and in a third series there was a reported survival of 75 of 100 implants (HeartMate®) [57]. A German retrospective study of 118 consecutive patients implanted with the Novacor® device reported an overall survival of 74% [12]. The CEDIT reviewers concluded that on average 70% of implanted cases would survive and proceed to transplantation. Of those transplanted, they estimated a 5-year survival of close to 90%, compared to a 70% 5-year survival for patients proceeding directly to transplantation [25].

5.3 COMPLICATION RATES

Because of changing anti-thrombotic and anti-infection protocols, changes in pump design, absence of controlled studies and changing medical management, any precise comparison of the rates of adverse events in patients supported by LVADs with those treated conservatively is not possible. Furthermore, many of the adverse events experienced in the early post-operative period, such as right ventricular failure and renal and hepatic failure, are reflections of the severity of the pre-operative status and will vary with the severity of the cases selected. More clearly attributable to LVAD technology are the complications of hemorrhage, thromboembolism and infection.

5.3.1 Hemorrhage

Major hemorrhage in the peri-operative period requiring re-operation is reported to occur in 20 to 44% of implant procedures [4, 17, 55]. The causes of such frequent hemorrhages include hepatic dysfunction, poor nutrition status, cardiopulmonary bypass induced platelet dysfunction, and the extensive nature of the surgery [17]. With the HeartMate® devices, which do not require anti-coagulation, hemorrhage outside the peri-operative period is not a problem. With use of the Novacor® device which requires anti-thrombotic therapy, later hemorrhage is observed, but is reported to be uncommon since the adoption of a new anti-thrombotic regimen, the "Chicago protocol" (personal communication from Dr. Portner: see note 3).

5.3.2 Thromboembolism

The rate of thromboembolic events is a variable which is partly pump-dependent. Rates from 5% (0.014 events per patient month) [42] to 15% [43] have been reported in two series using the HeartMate® device. Thromboembolism has been a more frequent complication of use of the Novacor® LVAD with rates ranging from 10 to 37% [33]. In one study of 36 patients supported for 109 ± 88 days, clinical cerebral embolism was evident in 17 (47%) [52]. However, these authors subsequently reported a lower incidence of this complication (one transient ischemic attack, TIA, in 9 procedures) following the addition of platelet inhibitors to the anti-coagulant regimen [51]. Recently introduced changes in pump design are reported to have lowered the frequency of this complication to 12% in a recent series of 155 patients[4]. The lower rates of 5% (HeartMate®) and 12% (Novacor®) probably better reflect the incidence to be expected at this time. The risk of this complication persists but diminishes with time.

5.3.3 Infections

Infections are common in LVAD recipients. Each of 13 patients supported for an average 127 days by an LVAD (HeartMate® or Thoratec®) had at least one infection [20]. In a study by the same group of 14 HeartMate® and 24 Thoratec® implants supported for a total of 2,572 days, there were 43 device-related infections in 11 patients. They occurred at a fairly constant rate throughout the period of LVAD support [19]. These infections are most frequently related

[4] Information provided by P.M. Portner, MD, Stanford University School of Medicine, Stanford, CA, USA, 1999.

to the exit site of the device's driveline, reportedly occurring at this site in from 22 to 33% of procedures [18, 28, 55]. Usually, they are controllable but in rare cases they may require device removal [17].

Argenziano et al found that 45% of 60 implanted patients developed significant infections after LVAD (HeartMate®) implantation [2]. Eight (13%) involving the driveline were distributed evenly between the first and twenty-seventh week of support. Eight (16%) developed endocarditis at a rate of 0.04 cases per month of support. Oz et al, who followed up 55 LVAD implants for over 2 months, found that 53% developed clinically significant infections. Infection of the device (LVAD endocarditis) occurred in 8, causing death in 4 [42]. Three of the four infections of the device were fatal in the report of Holman et al. [21]. Overall, although this complication diminishes with time, the rate remains significantly elevated [2, 20].

In evaluating these rates, it must be remembered that such patients in advanced heart failure, debilitated, and subject to frequent intravascular interventions, would have had a significant infection rate even in the absence of any VAD implant. Thus, in a study of the Novacor® device involving 156 implanted patients and 35 matched (but not randomized) controls, the infection rate was 66% in the former and 46% in the latter group [4].

Overall, these complications are a serious and on-going problem. It appears that significant infection is to be expected at some time in at least half of LVAD-supported patients and that about half of these involves the driveline. In the Novacor® study, the linearized rate of all complications experienced after 180 days of support was still 0.49/patient/month [29], and in a European study of 17 LVAD-implanted patients who had spent over 1 year at home, systemic infection occurred in 17.6% [24]. Almost all of these can be managed successfully. LVAD endocarditis is much less frequent but when it does occur usually involves re-operation and is often fatal.

5.4. Quality of Life of Long-Term LVAD Recipients

From the foregoing descriptive data, it appears that in the context of almost certain death, the discomfort and complications of short-term LVAD support are clearly acceptable. However, the longer the devices remain implanted, the more does the quality of life of the recipient bear on the decision whether to use an LVAD or not.

There is now considerable experience of long-term LVAD use with evidence of a health status adequate to permit near normal life for some. In a Swedish report, 3 of 6 patients supported by the HeartMate® VE device were at home for periods of 101 to 175 days before transplantation, enjoying "an active physical and social life" [30].

In a follow-up of 156 implants (Novacor®) carried out in 22 US centres, with an average duration of 97 days (maximum 780 days) [29], approximately 40% have been supported at home, many taking part in normal activities and some returning to work[5]. Myers et al reported on the status of 29 patients supported by an LVAD (HeartMate®) for an average of 194 ± 138 days. Twenty-one were discharged home, of whom fifteen were readmitted for various problems, six of which were device-related. No deaths occurred outside the hospital [40]. Catanese et al followed-up 14 patients on LVAD (HeartMate®) support for an average of 117 ± 24 days. None died and all were able to safely maintain their devices while 7 patients were discharged home [5].

[5] Information provided by P.M. Portner, MD, Stanford University School of Medicine, Stanford, CA, USA, 1999.

In a recent report of 25 European patients supported by an LVAD (Novacor®) for a median of 1.6 years, the median time spent outside the hospital was 1.38 years (88%). Most patients were able to resume normal activity and some returned to work [24]. From such a descriptive series it would appear that many long-term patients can live at home much of the time and pursue a fairly active, though not normal, life.

In a study using structured quality of life (QOL) assessments, the QOL of 120 out-of-hospital LVAD-supported patients was comparable to that of transplant recipients and superior to that of matching patients awaiting transplantation [11].

Moscowitz et al studied quality of life in patients before and during LVAD support and after cardiac transplantation, using the patients' estimates of utilities (range 0-1) arrived at by standard gamble. Average utilities were, before and during LVAD support, 0.548 and 0.809 respectively, compared to 0.964 after transplantation. These results suggest a quality of life on LVAD support which is substantially better than that on medical therapy alone, but not as good as after transplantation. These results suggest a quality of life on LVAD support which is substantially better than that on medical therapy alone, but not as good as after transplantation [36]. In a study of 35 patients at 60 and 90 days reported by Kormos, 97% of patients reported "better functioning" and the same percentage said they would "agree to the device for a relative" [28].

The psychological stress of long-term support on an LVAD must be considerable. Shapiro et al., after reviewing 30 procedures in one centre, found psychiatric interventions to be frequently necessary and "aggressive treatment of depression" to play a major role in improving functional status [54].

In summary**,** available evidence on the quality of life of patients on long-term LVAD support suggests that in spite of the continuing risk of infective or thromboembolic episodes and the burden of caring for the equipment, when used in the context of shortly anticipated death due to advanced heart failure, the complication rates and quality of life are acceptable.

6. COSTS OF IMPLANTATION

The costs under consideration are the direct costs to the health care system. The assumption is made that the technology will be applied in a Quebec hospital which is already undertaking cardiac transplantation. To simplify discussion of the costs of LVAD technology, US and UK cost estimates will be converted to Canadian dollars assuming 1 C$ = 0.65 US$ and 0.42 £ sterling, respectively. All cost estimates will be presented in 1998 Canadian $ values, adjusted when necessary according to the consumer price index [56], and rounded where appropriate.

No study has been made of the costs of LVAD technology in the Canadian health care system. In the USA, Gelijns et al studied the costs of LVAD implants (HeartMate®) in 12 patients. They found that the sum of all the direct costs of LVAD implantation (excluding device-related costs) up to the time of hospital discharge was approximately C$113,740 [16]. The Wessex Institute study estimated this cost at $22,569 [61]. It is hard to estimate how much this would cost in the Canadian system. Gelijns et al. and the CEDIT reviewers both conclude that the cost of LVAD implantation is comparable to the costs of cardiac transplantation. An estimate of the cost of cardiac transplantation in Quebec was approximately $48,443 (adjusted to 1998 $) [7], or 43% of the US cost of LVAD implantation as estimated by Gelijns and colleagues. This estimate is close to that of the UK study, $50,760 [61], and will be assumed to be the cost of LVAD implantation in Quebec.

The HeartMate® and Novacor® devices cost approximately $94,000 [58] and $90,000[6]. Thus the total cost of a Novacor® implantation would be $138,443. The hospital monitor, costing $62,000, and the personal monitors costing $31,000 each (according to Dr. P.M. Portner) are re-usable, and their costs are not considered in these estimates. The number of re-uses can only be guessed at. f the former were used for 30 patients and the latter for 5, approximately $7,000 should be added to the cost of each implantation.

The costs of maintaining a patient after successful LVAD implantation (the average costs of physicians fees, medications, hospital admissions) was found by Gelijns et al to be (in $C) $77 per day, including the cost of hospital readmissions. The likely cost of post-implant maintenance in the Canadian setting is unknown. In the Wessex Institute study, because no data were available, it was, surprisingly, decided to consider follow-up to be without cost [61]. As a first approximation, we will assume that the average Canadian maintenance costs would be 50% of the US costs as estimated by Gelijns et al, or $38 per day. Assuming an average of 100 days on LVAD support before transplantation, the cost in Canada of maintaining a patient prior to transplant would be $3,800. This is a relatively small component of the total cost. If maintenance actually cost 50% more or less than estimated, this value would be $7,600 or $1,900, respectively.

Based on the above assumptions, when used in the emergency context in which the alternative would be death within days, and assuming 70% survival of those implanted and support for an average of 100 days before transplantation, this technology would increase the cost of each transplantation by [($138,443 x 100) + ($3,800 x 70)] ÷ 70 = $201,576 ($205,376 to $199,676 varying maintenance costs ± 50%).

[6] Information provided by P.M. Portner, MD, Stanford University School of Medicine, Stanford, CA, USA, 1999.

7. COST-EFFECTIVENESS

It is clear from the above that reliable estimates of cost-effectiveness cannot be made on the basis of these data. However, it is possible to assume scenarios which, in light of the available information, seem reasonable as a basis for estimation of cost-effectiveness. First of all, the cost-effectiveness will depend on which application of LVADs is being considered.

7.1 APPLICATION 1: BRIDGE TO TRANSPLANT

7.1.1 Emergency Implantation

Let us first assume that LVADs will only be used as a bridge to transplant, and only in the context of emergency implantation when imminent death due to heart failure is virtually certain and no donor organ is available. Considered in this context, this technology might at first be considered to be acceptably cost-effective. However, it must be remembered that there are already too few donor hearts to meet the demand. Thus use of a donor heart for a patient whose life has been saved by LVAD use will automatically deprive some other potential recipient on the transplant waiting list. Accordingly, as long as LVADs are used only as a bridge to transplant, they will save no additional lives. They will only save different lives, rendering estimation of cost-effectiveness impossible.

7.1.2 Elective Implantation

If used electively for patients awaiting transplantation, life years may be saved because interim LVAD support of severely compromised patients allows for better planning of cardiac transplantation, with an improved patient status and better transplant survival rates. The extent of this potential improvement in transplantation outcome will vary according to the clinical status of the patients concerned and is accordingly hard to predict. There are no randomized controlled series. The nearest to a controlled study is series of bridge to transplant LVAD (Novacor®) implants reported by Portner, in which the survival at one year after transplant of patients receiving prior LVAD support was 91%. This was compared by the authors to a rate of 77% without support, derived from the pooled ISHLT data[7].

The CEDIT reviewers estimated that a period on LVAD support prior to transplantation would be expected to raise the 5 year *post-transplant* survival rate from 70% to close to 90% [25]. This estimate must be based on slender data. But if correct, it would suggest that judicious elective use of LVAD technology might increase survival after transplantation by 15 to 20 percentage points. Even based on the upper value, it would still, however, be a relatively cost-ineffective technology.

Let us consider a scenario which compares 100 patients transplanted with prior LVAD support to 100 who are transplanted directly with the following assumptions.

- That 70% of LVAD recipients proceed to transplant. To prepare 100 patients for transplant, 143 LVADs must be implanted.
- That of 100 transplant recipients who have had prior LVAD-assist, 20 will survive who would have died in the absence of LVAD support.
- An average 100 days on LVAD support.
- Survival rate 1 month post- transplant : 95% (93 to 96% according to age) [59].
- Average survival time after transplantation : 13 years. This was the estimate used in the

[7] Information provided by P.M. Portner, MD, Stanford University School of Medicine, Stanford, CA, USA, 1999.

Quebec study [7]. It was based on a projected 74% survival at 3 years. The contemporary observed rate of the ISHLT [23] is almost identical.

- Average annual cost after transplantation : $10,000. The average annual cost in the Quebec study, in 1998 adjusted dollars, is $10,350 [7].

Then:

- The health benefit would be survival of 20 patients x 13 years = 260 life years.
- The marginal cost would be the cost of 143 implant procedures ($48,443 + $90,000) x 143 = $19,797,349.

  Plus the cost of maintaining 100 implant survivors for an average of 100 days ($3,800 x 100) = $380,000.

  Plus the cost of transplanting and maintaining an additional 20 transplant survivors for an average of 13 years ($48,443 x 20) +($10,000 x 20 x 13) = $3,568,860.

  The total cost added by these 143 implantations amounts to $ 23,746,209.

Thus, the resultant cost-effectiveness of this scenario would thus be $91,332 per year of life (undiscounted), or $117,197 discounted at 5%.

However, it may be optimistic to expect 70% survival after emergency implantation [50] and, as discussed above, the estimated 20% improvement in transplant survival rate due to prior LVAD support may also be too high. Both of these possible over-estimates would result in under-estimation of the cost per life year saved.

On the other hand, when used electively for patients on the transplant waiting list the implantation of an LVAD may save some of the costs of medical management of patients awaiting transplantation who do not receive LVAD support. These will vary from modest medication costs to intermittent hospitalization. Their inclusion would slightly reduce this estimated cost per year of life saved.

These estimates also take no account of how many patients might have lived, and for how long, in the absence of elective implantation. This figure will be highly dependent on case selection. In Quebec, from 10-17% of patients on the waiting list die each year [47]. If case selection were such that of 100 comparable cases, 75 would have lived on average 1 year in the absence of LVAD support, the years of life saved by the procedure would be reduced from 206 to 185, with a resultant cost-effectiveness of $126,304 per year of life, or $185,980 when discounted.

7.2 Application 2: Bridge to Recovery

Emergency Implantation. If it were possible to predict which cases would recover cardiac function as a result of a period of LVAD support, the procedure would be considerably more cost-effective. Unfortunately this is not yet possible, and this outcome seems at present to be unlikely in more than 5% of procedures [9, 14, 32].

7.3 Application 3: Permanent Alternative to Transplant

Several authors have suggested that this technology is now sufficiently advanced to allow the application of LVADs as a permanent substitute for the failed ventricle [6, 42, 44]. A randomized controlled trial of long-term LVAD support versus optimal medical treatment, REMATCH, is currently underway [48].

The data on which to base estimates of either the possible health benefits or the costs, in the Canadian context, of this application of LVAD tech-

nology are even less adequate. However, some idea of the possible cost-effectiveness of this use of the technology can be arrived at according to its application, on the basis of the following assumptions.

7.3.1 Emergency Implantation

- Assume that the technology is first restricted to emergency cases in which death would shortly occur in its absence.

- Assume that the foregoing estimates of costs of implantation and maintenance of LVADs are valid, that 70% of patients will survive LVAD implantation with a subsequent mortality of 3% per year, and that LVADs will require replacement every 4 years with an operative mortality of 10%. The current average annual post-transplant mortality rate from the ISHLT from year 1-5 is 3.68% [23].

- Assume the cost of replacing the LVAD at 4 years is the same as the first implant.

With these assumptions, it can be estimated that carrying out 100 LVAD implants in such critically ill patients would, by the end of the 12th year, have cost $38,362,221 with a gain of 641 years of life, for an estimated cost-effectiveness of $59,842 per year of life (undiscounted), or $57,628 discounted at 5%.

The above estimate assumes rapid demise, with negligible cost, as the outcome in the absence of LVAD implantation. If it were assumed that in the absence of LVAD use, patients would receive short-term support using balloon counterpulsation or a centrifugal pump, each LVAD implant would save this cost. If we assumed that such support for 11 days might cost approximately $50,000 per patient (Appendix 1), this would reduce the net cost per 100 LVAD procedures by $5,000,000, resulting in an estimated cost-effectiveness (by 12 years) of $52,043 per life year or $50,075 discounted at 5%.

7.3.2 Elective Implantation

If used electively to save deteriorating heart failure patients for whom no donor heart is available, it must be assumed that some of the subjects receiving LVADs would have survived for some months or years in the absence of an implant. If, for example, we assume there would have been an average 1 year survival without LVAD support, the life years gained would be reduced to 531, with a consequent estimate of cost-effectiveness at 12 years of $70,903 (or $67,883 discounted at 5%), per life year.

7.4 SUMMARY

It can be seen that estimates of cost-effectiveness of use of this technology are highly variable depending on the circumstances of use and the assumptions made for each estimate. Considering only direct costs to the health care system, and without sensitivity analysis of many of the input variables, we arrive at the following estimates:

- Bridge to transplant, *emergency interventions:* No estimate possible because, due to limited donor hearts, such use will not save additional lives.

- Bridge to transplant, *elective interventions:* from $91,000 (discounted $117,000) to $126,000 (discounted $186,000) per life year.

- Permanent alternative to transplantation, *emergency use*: $52,000 (discounted $50,000), to $60,000 (discounted $58,000); *elective use:* $71,000 (discounted $68,000).

It must be stressed that these are estimates based on hypothetical scenarios. They are carried out to give decision-makers some idea of the order

of cost-effectiveness which might be associated with use of this technology. No comparison can be made between these estimates and the estimate of the Wessex Institute [61].

8. ECONOMIC IMPACT

The total cost to the health care system of the introduction of this technology will depend substantially on the application for which it is used, the restrictiveness of the utilization guidelines adopted, and the rigor with which they are applied.

8.1. APPLICATION 1: BRIDGE TO TRANSPLANT

Both the French and Oregon evaluations have recommended that LVADs only be used for the bridge to transplant application. Strict adherence to this recommendation would mean that the number of LVADs used would not be permitted to exceed the number of donor hearts available for transplantation. At present in Quebec, this figure is between 30 and 50 per year [47]. If, under emergency circumstances LVADs were used before 10 transplant procedures each year, the total cost would be the cost of implant surgery ($48,443) + the device ($90,000) x 10, plus the maintenance costs of 7 survivors for 100 days ($3,800), or approximately $1.4 million per year, exclusive of transplantation costs. To this could be added some fraction of the cost of the hospital monitor ($62,000) and 10 personal monitors ($31,000) re-usable perhaps for 7 years, or $53,000 per year.

However, the difficulty in practice of strict adherence to a bridge to transplant application must be recognized from the beginning. Some patients—in one series as many as 20% [46] — prefer not to proceed to transplant. Of the remainder, these relatively healthy individuals on LVAD support will soon find themselves in competition for the limited number of donor hearts with the iller and more urgent heart failure cases. Indeed, it may well be considered ethically unacceptable to award the available donor heart to a relatively healthy individual who is already satisfactorily supported by LVAD, and, in so doing, allow another unsupported patient to die. If this prediction is correct, the number of surviving LVAD implants will inevitably increase in spite of the best of intentions to restrict their use to bridge to transplant applications, and LVADs will, in effect, increasingly be used as long-term or even permanent replacements for the failed heart.

There is as yet no experience on which to base estimates of the average life of LVADs or of the number of times they can be successfully surgically replaced. However, the following scenario can give some idea of the possible economic impact of an increasing number of “permanent” implants:

- Assume arbitrarily that each year 10 LVADs are implanted, 7 survive and of these, 3 proceed to transplant and 4 become successfully and permanently maintained on an LVAD.

- Assume that on average each implant requires replacement every 4 years with a mortality of 10%.

- Assume, as previously estimated, that the average cost of implantation is $138,443 and the cost of maintenance of a patient on LVAD support for 1 year is $13,870.

By the end of the 12th year, such a program could result in 26 implant procedures per year (10 implants + 16 replacements) with maintenance of 23 long-term implant survivors, at a total cost in the order of $3.8 million per year.

Such scenarios are, of course, entirely hypothetical since the rapidly improving technology is likely to outdate these projections in much less than 12 years. However, it is clear that the an-

nual total cost of an ongoing program to implant 10 patients per year will increase progressively.

8.2. APPLICATION 3: PERMANENT ALTERNATIVE TO TRANSPLANT

With increasing general awareness of this option for individuals facing imminent death due to heart failure, it is unlikely that the same strict selection criteria presently used for heart transplantation will long be maintained to select patients for LVAD support. And with wider selection criteria the costs of application of this technology will become substantial.

How large is the potential LVAD recipient pool? The technology is already being successfully used for patients over 60 years of age [60]. According to Goldstein, "Recent estimates indicate that nearly 60,000 patients annually in the United States could benefit from heart transplantation or long-term mechanical support" [17]. On a proportional basis this would be the equivalent of approximately 1,776 new implants per year in Quebec.

In the State of Oregon (population 2.7 million), according to the evaluation of the Health Resources Commission, there are 25 patients per year who could benefit from LVAD implant technology using strict bridge to transplant criteria. Proportionately in Quebec, this would be the equivalent of approximately 68 patients per year. But the Commission members warn that if more generous criteria are accepted, including the use of LVADs as permanent interventions, the number of candidates appropriate for either LVAD or transplant could exceed 950 per year, the equivalent in Quebec of approximately 2,603 per year. Based on the previous cost estimates, to implant LVADs in only 1,500 new patients per year would, by the end of 12 years, involve an annual expenditure of the order of $570 million (with maintenance of 9,469 patients) (Appendix 2). While these projections rest on many hypotheses, it is clear that the economic impact of unrestricted use of LVADs would be substantial.

9. ETHICAL AND SOCIAL ISSUES

As will be clear by now, the question of the introduction of LVAD technology is beset by some unusually difficult questions. The very concept of individuals functioning in society with mechanical implanted hearts will require some getting used to. In deciding on the possible use of this technology, answers to the following questions must be sought.

9.1 ACCESS TO LVAD TECHNOLOGY

- Is it ethically acceptable in our health care system to refuse our citizens access to a technology, which has been shown to be capable of saving lives, on grounds of cost?

Judicious use of LVADs is clearly capable of saving lives when cardiogenic shock complicates myocardial infarction or cardiac surgery. In view of this, and in view of its increasing application elsewhere, it is doubtful whether this promising technology could or even should continue to be ignored in Quebec. *There is, therefore, a case at this time for at least some limited application of LVAD technology in Quebec.*

9.2 EXTENT OF APPLICATION

- If we decide that LVAD technology is now sufficiently developed for limited application, how narrow should these limits be?

There are two reasons why, if it is introduced, the number used should remain restricted. First, when an LVAD is used as a bridge to transplant, the recipient may be saved, but some other individual will be deprived of a donated heart, while the exercise will cost about $200,000 of societal resources (see Costs of Implantation, section 6). Clearly if this form of "life saving" is undertaken, it should not be an extensive undertaking.

Second, the introduction of the LVAD as a bridge to transplant will be followed by immense pressure to extend its use to prolong the life of all patients with terminal heart failure, regardless of the availability of cardiac donors**.** If this were to happen, the economic impact would be substantial. To finance LVAD use as a replacement for transplant for all appropriate heart failure patients would require a sum of the order of $570 million per year, or 4.7% of all health expenditures of the *Ministère de la Santé et des Services sociaux du Quebec* (Health Department) in 1999 [35]. Such a sum would be $100 million more than the present budget of the 5 hospitals making up the McGill University Health Centre in Montreal. Thus, although relatively cost-effective in relation to many other accepted technologies, the acceptance of liberal use of LVADs would involve such substantial opportunity costs that it should not be permitted at this time. For these reasons, *until there is good evidence of an increase in its clinical effectiveness and a substantial reduction in cost, any such extension of its application should not be allowed to take place.*

In addition, it should not be undertaken at all without a clear understanding that limitation of use will be essential, and with clear prior definition of these limits. Where these limits should be fixed is clearly a matter which will require frequent adjustment. But if apart from the rare case of probably reversible cardiomyopathy, it is accepted that at this time this technology should only be applied with the clear objective of bridge to transplant, it follows that *it should only be used for transplant-appropriate cases, when the need for intervention is urgent, and a donor heart is not available. As a first approximation these conditions might lead to LVAD use prior to 20% of transplants, or 10 per year. This is the number that might be approved initially*.

9.3 PRECEDENT

- Against such restricted use, it may be argued that there is already ample precedent for the commitment of resources to programs characterized by high cost and relatively poor cost-effectiveness. For example, in 1996 in Quebec, 1,832 patients with renal failure were maintained on hemodialysis [49], a procedure with an estimated cost-effectiveness of $85,312 per life year [8] at an annual cost of approximately $156,000,000. To be consistent, we should surely now approve funding for a comparable technology which maintains the lives of patients with heart failure?

In response, it must be remembered that previous commitment to programs such as renal dialysis were usually made long before it was realized how extensive the application of these technologies would be, and before there was any real understanding that our resources had limits. Today health care resources are clearly limited and we are surely committed to spend those that are available as wisely as possible. *To demand that we be consistent with such past decisions is not, therefore, logical. We cannot continue to ignore the cost-effectiveness, economic impact, and opportunity costs of our decisions or allow present policy to be driven by a desire for consistency with past decisions taken in a different context.*

9.4 INDIVIDUAL OR SOCIETAL VIEWPOINT?

- The duty of physicians to do their best for their individual patients has been recognized since Hippocrates. Physicians therefore should use whatever technology might help their patients, irrespective of costs. However, the society which contributes its resources surely has a right to expect the maximum health benefit for its investment. When allocating limited resources, *should the good of the individual or of society prevail?*

The tension between societal and individual needs, which pervades all resource allocation decisions, will never be finally resolved. However, while the allocation of *societal* resources must take account of cost-effectiveness, the physicians of *individual* patients cannot ethically do other than use *all* available technologies which are effective, however costly, if by so doing they can improve their patients' outcomes. The key word here is "available". In our health care system what is available is a societal decision. *To make it possible for physicians to be able to act according to their conscience, it is essential that societal decision-makers define in advance the resources which will be available for this purpose.*

9.5 EQUITY

- If strict limitation of the number of LVADs funded by the Quebec health system is successfully achieved, there will be strong pressures to undertake the procedure in the private sector. What will be our response to patients who have had LVADs implanted at their own expense, outside the country or in the private sector, but who can no longer afford the costs of maintenance and replacement? Should transfer from the private sector be permitted under these circumstances? Similarly, what will we do about patients who opt to stay within the publicly funded health system but offer to purchase the devices themselves? Should individuals be allowed to "jump the queue" in this way?

These equity issues must be addressed fairly urgently. Refusal by the health care system of the costs of maintenance of patients whose LVADs were implanted in the private sector or in the USA is difficult to envisage. In practice, the number of such patients will likely be small.

An offer by LVAD candidates to provide their own devices could reasonably be considered an attempt to "jump the queue" unfairly. However, the concept of a queue implies that the advance of one individual sets back the others. To the extent that surgery was not being delayed for lack of surgeons or of operating rooms, but because of the lack of the rationed device, individuals who provided their own devices would not be adversely affecting others. Thus it might be judged to be more unjust to refuse to install a device paid for by a patient, if such patient was an acceptable transplant candidate awaiting a donor heart. Furthermore, by their accepting an LVAD and thus being removed from the transplant waiting list, the life of another might be saved. This issue should be addressed before use of LVADs is authorized.

9.6 TRANSPARENCY

- Such questions as these have rarely been directly addressed in the past, except in the context of closed committee rooms. As a result, the general public and the journalists who inform it have little comprehension of the complexity and consequences of these decisions. The fact that resources are limited and that beneficial interventions must sometimes be refused for economic reasons will be extremely difficult to accept.

Nonetheless, unless governments decide to substantially and continually increase health care funding, the continuing development of new, effective, but expensive procedures and drugs will make it essential to limit some effective technologies. For the rational development of health policy this must be frankly admitted and discussed. *For the public to accept such decisions, a widened, more open decision-making process will be necessary. Failure to achieve this will make logical and fair policy development increasingly difficult.*

10. PRACTICAL AND ADMINISTRATIVE ISSUES

There are several practical and administrative issues which should be decided before this technology is introduced.

10.1 LVAD CENTRES

If it is decided to approve funding for a limited number of LVADs in Quebec, the health benefits will not be maximized unless the intervention is restricted at first to a single institution. By directing all cases to one centre, the rate of learning of the health team concerned will be maximized. Political considerations should not be allowed to diminish clinical effectiveness by authorizing too many centres to carry out too few procedures each year. *Initially, to maximise experience, implantable LVADs should be implanted in one centre.*

Since multi-system failure is frequently experienced by such patients, *access to all medical specialty services such as infectious diseases, renal, hepatic, hematology and immunology services, must be assured in any centre undertaking this technology.*

To facilitate transfer of such patients, it would be necessary to *maintain a heart failure unit in the implant centre, with appropriate beds and support staff.*

Since no centre will be able to finance such a program from their existing funds, *any decision to approve use of LVADs must be accompanied by appropriate funding.*

10.2 COMMUNICATION NETWORK

If initially the technology is restricted to one centre, it will be necessary to facilitate access of patients from all areas of Quebec. This will require that a close functional network is established with other cardiac surgery centres. To allow rescue of cases who cannot be maintained on balloon counterpulsation and to facilitate patient transfer, some surgical centres at greater distance from the implant centre should be equipped with less expensive short-term support devices such as the Abiomed BVS 5000®. The transfer of such critically ill patients is no simple matter. Decisions must usually be taken under conditions of great urgency. *Accordingly, there must be a functioning LVAD network with a good exchange of information and even of personnel, sufficient for there to be a thorough mutual understanding of issues such as case selection criteria.*

10.3 RESEARCH

In order to maximize the clinical and scientific dividends of such an undertaking the institutions involved should be required *to maintain a register to record the relevant clinical and cost data of every case, with all the rigor of a research study.* While randomization of cases will not be feasible, with the collaboration of network members, *a control series of matching patients who do not receive LVAD implantation must be created as a basis of comparison of clinical outcomes and costs with LVAD recipients.*

10.4 REVIEW

The results of these studies should be made available annually to the health authorities and health professionals of Quebec and should be periodically (at 3 years maximum) evaluated with the help of external reviewers. At such time, it may be found appropriate to open a second implant centre or to make other modifications. *Poor clinical results or failure to deliver the research data should be considered cause for revision of policy.*

10.5 FUTURE DEVELOPMENTS

The technology of long-term mechanical circulatory support is in a state of explosive development. Numerous devices, including one developed in Canada [39], are in an advanced stage of development. These are smaller, potentially more reliable, and because they can be totally implanted with transcutaneous power transmission, are less likely to become infected. Thus, increasing clinical effectiveness and possibly lower costs may soon render many conclusions of the present report questionable. *It is recommended that within 12 months of the end of data collection (December 1, 1999) the conclusions of this report should no longer be accepted without verification.*

11. CONCLUSIONS

The implantable LVAD is a rapidly developing technology. It can no longer be considered "experimental" nor is it yet "accepted". There is a case for its *limited* application in Quebec under *close surveillance.*

- At this time, it should only be used with the following indications:
  - with the objective of subsequent transplantation only
  - in transplant-appropriate cases
  - when need for intervention is urgent
  - when a donor heart is not available.

- With acceptance of these indications, approximately 10 implants might be required in the first year.

- Until there is a substantial increase in the clinical effectiveness and a reduction in costs, wider application of LVAD technology would result in inappropriate use of resources and should not be allowed to occur.

- This technology may prove to be appropriate for hundreds of patients, and to limit its application may be extremely difficult. It is essential that the resources which will be made available for LVADs be defined in advance.

- Initially, implantable LVAD technology should be confined to one centre in which a heart failure unit must be maintained to receive appropriate patients from other centres.

- To facilitate access to the centre, a good communication network must be established, and less expensive, non-implantable LVAD technology must be acquired by some distant centres.

- Initially, the designated implant centre should record and publish all relevant clinical and cost data. Results should be subject to external review at least by 3 years.

- A decision to use LVADs must be accompanied by appropriate funding.

- It will be important to define in advance our attitude to individuals who offer to pay for their own device, and those who have an LVAD installed in the private sector but cannot afford the maintenance or replacement costs.

Access to an effective technology has not, at least until recently, previously been limited on grounds of its cost. Until the opportunity costs of such decisions (i.e. what we must do without in order to pay for a technology like LVADs) are understood and widely accepted, wise decisions will be difficult to make and apply. In order for the public to comprehend and accept these decisions, there must be widespread and open debate of the fundamental issues raised by allocation of collective resources.

APPENDIX 1:
COSTS OF ALTERNATE MANAGEMENT

If it were assumed that the alternative to an emergency LVAD implant was not sudden death but short-term support in the intensive care unit using balloon counterpulsation or a centrifugal pump, this would generate costs which would be avoided by use of an implant. In a 1996 US study of 1,279 patients receiving an average 2.9 days support with a centrifugal pump, the average cost was US$167,000 (C$257,000) [26]. in 1998, the maintenance of a single patient on such support for 11 days was estimated to cost $50,000 [27].

APPENDIX 2:
ESTIMATION OF THE ECONOMIC IMPACT OF "PERMANENT" LVAD IMPLANTS

Estimation of economic impact, after 12 years, of a scenario in which 1,500 new "permanent" LVAD implants are carried out each year, assuming:

- Implant surgery and re-implant surgery each cost $138,443.
- Survival rate of first implantation is 70%.
- Survival rate of re-implantation is 90%.
- Annual mortality rate of implant survivors is 3%.
- Annual cost of maintaining one implant patient is $13,870.
- Time between implants (device life) is 4 years.

Then:

Implant procedures in year 12 = 1,500 new implants + 930 first replacements + 741 second replacements	=	3,170 procedures
Survivors at end of year 12	=	9,469 survivors
Costs in year 12	=	$570,231,667
Cumulative life years added at end of year 12	=	67,600 years
Cumulative costs at end of year 12	=	$4,869,252,633

REFERENCES

1. Adamson RM, Dembitsky WP, Jaski BE, Daily PO, Moreno R, Kim JC, Sono J, Akasaka T, Hoagland PM, Gordon JB. Left ventricular assist device support of medically unresponsive pulmonary hypertension and aortic insufficiency. ASAIO J 1997;43: 365-9.

2. Argenziano M, Catanese KA, Moazami N, Gardocki MT, Weinberg AD, Clavenna MW, et al. The influence of infection on survival and successful transplantation in patients with left ventricular assist devices. J Heart Lung Transplant 1997;16:822-31.

3. Ashton RC JR., Goldstein DJ, Rose EA, Weinberg AD, Levin HR, Oz MC. Duration of left ventricular assist device support affects transplant survival. J Heart Lung Transplant 1996;15:1151-7.

4. Baxter Healthcare Corporation. Physicians's Manual. Novacor LVAS. Catalogue no. N20072. Oakland (California, USA): Baxter Healthcare Corporation; 1998.

5. Catanese KA, Goldstein DJ, Williams DL, Foray AT, Illick CD, Gardocki MT, et al. Outpatient left ventricular assist device support: a destination rather than a bridge. Ann Thorac Surg 1996;62:646-53.

6. Chillcott SR, Atkins PJ, Adamson RM. Left ventricular assist as a viable alternative for cardiac transplantation. Crit Care Nurs Q 1998;20:64-79.

7. Conseil d'évaluation des technologies de la santé du Québec (CETS). Hémodialyse et dialyse péritonéale: Analyse comparative des rapports coût-efficacité. Montréal (Québec, Canada): CETS; 1998.

8. Conseil d'évaluation des technologies de la santé du Québec (CETS). La transplantation cardiaque au Québec: Le taux de survie, les coûts et le rapport coût-efficacité. Montréal (Québec, Canada): CETS; 1992.

9. DeRose JJ, Argenziano M, Sun BC, Reemtsma K, Oz MC, Rose EA. Implantable left ventricular assist devices: an evolving long-term cardiac replacement therapy. Ann Surg 1997;226:461-8.

10. DeRose JJ, Umana JP, Argenziano M, Catanese KA, Levin HR, Sun BC, Rose EA, Oz MC. Improved results for postcardiotomy cardiogenic shock with the use of implantable left ventricular assist devices. Ann Thorac Surg 1997;64:1757-63.

11. Dew MA, Kormos RL, Winowich S, Nastala CJ, Borovetz HS, Roth LH, et al. Quality of life outcomes in left ventricular assist system inpatients and outpatients. ASAIO J 1999; 45(3):218-25.

12. El-Banayosy A, Deng M, Loisance DY, Vetter H, Gronda E, Loebe M, Vigano M. The European experience of Novacor left ventricular assist (LVAS) therapy as a bridge to transplant: a retrospective multicentre study. Eur J Cardiothorac Surg 1999; 15(6): 35-41.

13. Frazier OH, Macris MP, Myers TJ, Duncan JM, Radovancevic B, Parnis SM, Cooley DA. Improved survival after extended bridge to cardiac transplantation. Ann Thorac Surg 1994;57(6):1416-22.

14. Frazier OH, Myers TJ, Radovancevic B. The Heartmate left ventricular assist system. Overview and 12-year experience. Tex Heart Inst J 1998;25:265-71.

References

15. Frazier OH, Rose EA, McCarthy P, Burton NA, Tector A, Levin H, et al. Improved mortality and rehabilitation of transplant candidates treated with a long-term implantable left ventricular assist system. Ann Surg 1995;222:327-36.

16. Gelijns AC, Richards AF, Williams DL, Oz MC, Oliveira J, Moskowitz AJ. Evolving costs of long-term left ventricular assist device imlantation. Ann Thorac Surg 1997; 64:1312-9.

17. Goldstein DJ, Oz MC, Rose EA. Implantable left ventricular assist devices. N Engl J Med 1998;339:1522-32.

18. Griffith BP, Kormos RL, Nastala CJ, Winowich S, Pristas JM. Results of extended bridge to transplantation: window into the future of permanent ventricular assist devices. Ann Thorac Sur 1996;61:396-8.

19. Holman WL, Bourge RC, Spruell RD, Murrah CP, McGiffin DC, Kirklin JK. Ventricular assist devices as a bridge to cardiac transplantation. A prelude to destination therapy. Ann Surg 1997;225:695-706.

20. Holman WL, Murrah CP, Ferguson ER, Bourge RC, McGiffin DC, Kirklin JK. Infections during extended circulatory support: University of Alabama at Birmingham experience 1989 to 1994. Ann Thorac Surg 1996;1:366-71.

21. Holman WL, Skinner JL, Waites KB, Benza RL, McGiffin DC, Kirklin JK. Infection during circulatory support with ventricular assist devices. Ann Thorac Surg 1999;68(2):711-6.

22. Hunt SA, Frazier OH, Myers TJ. Mechanical circulatory support and cardiac transplantation. Circulation 1998;97:2079-90.

23. International Society for Heart and Lung Transplantation (the). Sixteenth Annual Data Report. Avalable: URL: http://www.ishlt.org/registry.html.

24. Jansen PJM, Wheeldon, Portner PM. Long-term home discharge support with Novacor LVAS. J Heart Lung Transpl 1999;18:67-68.

25. Jouveshomme S, Baffert S, Fay A-F. Coeur Artificiel (III). Dossier CEDIT. Paris: Assistance Publique – Hôpitaux de Paris; September 1998.

26. Joyce LD, Kiser JC, Eales F, King RM, Overton JW Jr, Toninato CJ. Experience with generally accepted centrifugal pumps: personal and collective experience. Ann Thorac Surg 1996;61(1):287-90.

27. Kaplow M. Mechanical circulatory support. Cost study. Montreal (Quebec, Canada): Department of Quality Assurance, McGill University Health Centre; 1998.

28. Kormos RL. Unresolved issues in long-term mechanical circulatory support. International Society for Heart and Lung Transplantation. Conference on Mechanical Cardiac Support and Replacement. Atlanta (USA). November 5-6, 1999.

29. Kormos RL, Ramasamy N, Sit S, Cleeland AD, Jassawala JS, Portner PM. Bridge-to-transplant (BIT) experience with the Novacor left ventricular assist system (LVAS): Results of a multicenter US study. J Heart Lung Transpl 1999;18:1-63.

30. Koul B, Solem JO, Steen S, Casimir-Ahn H, Granfeldt H, Lönn UJ. Heartmate left ventricular assist device. Ann Thorac Surg 1998;65:1625-30.

References

31. Levin HR, Oz ML, Chen JM, Packer M, Rose EA, Burkhoff D. Reversal of chronic ventricular dilatation in patients with end-stage cardiomyopathy by prolonged mechanical unloading. Circulation 1995;91: 2712-20.

32. Mancini DM, Beniaminovitz A, Levin H, Catanese K, Flannery M, DiTullio M, et al. Low incidence of myocardial recovery after left ventricular assist device implantation in patients with chronic heart. Circulation 1998;80(2):145-9.

33. McCarthy PM, Sabik JF. Implantable circulatory support devices as a bridge to heart transplantation. Seminars in Thorac Cardio Surg 1994;6:174-80.

34. McCarthy PM, Smedira NO, Vargo RL, Goormastic M, Hobbs RE, Starling RC, Young JB. One hundred patients with the Heartmate left ventricular assist device: evolving concepts and technology. J Thorac Cardiovasc Surg 1998;115:904-12.

35. Ministère de la Santé et des Services sociaux du Québec (MSSS). Crédits consacrés à la santé et aux services sociaux du Québec selon la nouvelle structure budgétaire, en 1998-99 et 1999-2000. Source: SAS, MSSS, August 1999. Available: URL: http://www. msss.gouv.qc.ca/fr/ statisti/indicat/depenses/ niveau5/index4.htm.

36. Moskowitz AJ, Weinberg AD, Oz MC, Williams DL. Quality of life with an implanted left ventricular assist device. Ann Thorac Surg 1997;64:1764-9.

37. Muller J. Lessons learned from patients after weaning from LVAD: Four years of experience and follow-up. International Society for Heart and Lung Transplantation. Conference on Mechanical Cardiac Support and Replacement. Atlanta (USA). November 5-6, 1999.

38. Muller J, Wallukat G, Weng YG, Dandel M, Spiegelsberger S, Semrau S, et al. Weaning from mechanical cardiac support in patients with idiopathic dilated cardiomyopathy. Circulation 1997;96: 542-9.

39. Mussivand T, Hendry PJ, Masters RG, King M, Holmes KS, Keon WJ. Progress with the HeartSaver ventricular assist device. Ann Thorac Surg 1999;68(2):785-9.

40. Myers TJ, Catanese KA, Vargo RL, Dressler DK. Extended Cardiac Support with a portable left ventricular assist system in the home. ASAIO J 1996;42:M576-9.

41. Oregon Health Resources Commission. Medical technology assessment and health resources plan for ventricular assist devices. Oregon Health Plan Policy and Research. Health Resources Commission. October 9, 1998. Available: URL: http://ohpr.state.or. us/hrc/vad.html.

42. Oz MC, Argenziano M, Catanese KA, Gardocki MT, Goldstein DJ, Ashton RC, et al Bridge experience with long-term implantable left ventricular assist devices. Are they an alternative to transplantation? Circulation 1997;95:1844-52.

43. Pae W. Thoratec and Thermo Cardio Systems Pneumatic left ventricular systems as a bridge to transplant: An institutional experience. Conference on Mechnical Cardiac Support and Replacement. International Society for Heart and Lung Transplant. Atlanta (USA). November 5-6, 1999.

44. Piccione W Jr. Mechanical circulatory assistance: Changing indications and options.

J Heart Lung Transpl 1997;16 Suppl:S25-S28.

45. Poirier VL. Worldwide experience with the TCI HeartMate system: issues and future perspective. Thorac Cardiovasc Surg 1999; 47 Suppl 2:316-20.

46. Portner PM. Novacor Left Ventricular Assist System. International Society for Heart and Lung Transplantation. Conference on Mechanical Cardiac Support and Replacement. Atlanta (USA). November 5-6, 1999.

47. Québec-Transplant. Annual Report 1998. Montreal (Quebec, Canada): Quebec Transplant; 1998.

48. Rose EA, Moskowitz AJ, Packer M, Sollano JA, Williams DL, Tierney AR, et al. The REMATCH trial: rationale, design, and end points. Ann Thorac Surg 1999;67:723-30.

49. Schaubel DE, Morrison HI, Desmeules M, Parsons DA, Fenton SSA. End-stage renal disease in Canada: prevalence projections to 2005. CMAJ 1999;160:1557-63.

50. Schmid C, Deng M, Hammel D, Weyand M, Loick HM, Scheld HH. Emergency versus elective/urgent left ventricular assist device implantation. J Heart Lung Transplant 1998;17(10):1024-8.

51. Schmid C, Weyand M, Hammel D, Deng MC, Nabavi D, Scheld HH. Effect of platelet inhibitors on thromboembolism after implantation of a Novacor N100 – preliminary results. Thorac Cardiovasc Surg 1998;46: 260-2.

52. Schmid C, Weyand M, Nabavi DG, Hammel D, Deng MC, Ringelstein EB, Scheld HH. Cerebral and systemic embolization during left ventricular support with the Novacor N100 device. An Thorac Surg 1998; 65:1703-10.

53. Schocken DD, Arrieta MI, Leaverton PE, Ross EA. Prevalence and mortality rate of congestive heart failure in the United States. J Am Coll Cardiol 1992;20:301-6.

54. Shapiro PA, Levin HR, Oz MC. Left ventricular assist devices. Psychosocial burden and implications for heart transplant programs. Gen Hosp Psychiatry 1996;18 Suppl:S30-S35.

55. Smedira MG. 200 Implantable LVADs: Have things change since the first 100? International Society for Heart and Lung Transplantation. Conference on Mechanical Cardiac Support and Replacement. Atlanta (USA). November 5-6, 1999.

56. Statistics Canada. Consumer prices and price indexes. Catalog 62-010, Ottawa: Statistics Canada; 1998.

57. Sun BC, Catanese KA, Spanier TB, Flannery MR, Gardocki MT, Marcus LS, et al. 100 long-term implantable left ventricular assist devices: the Columbia Presbyterian interim experience. Ann Thorac Surg 1999; 68(2):688-94.

58. Thermo Cardiosystems Inc. Worlwide registry September 1999. Thermo Cardio Systems Inc.: Woburn, Mass (USA); 1999.

59. United Network for Organ Sharing. Patient survival rates at one month and at one, three and five years. Table 40. Heart Transplants. UNOS. Available at: http:// www.unos.org/data/anrpt98/a98_table40_01_hr.htm.

60. Van Meter CH Jr, Smart FW, Stapleton DD, Ventura HO, Ochsner JL. Mechanical

assistance of the failing heart in the elderly. Cardiol Elderly 1999;160:1557-63.

61. Wessex Institute for Health Research and Development (the). Left ventricular assist devices (LVADs) for end-stage heart failure. Development and Evaluation Committee Report No. 103. September 1999. Available: URL: http://www.epi.bris.ac.uk/ rd.